Clin Physiol Funct Imaging (2012) 32, pp445–454 doi: 10.1111/j.1475-097X.2012.01148.x

Effects of exercise prescription on daily physical activity and maximal exercise capacity in coronary artery disease patients with and without type 2 diabetes

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Summary

Background: Promotion of and adherence to increased physical activity (PA) is an important part of the prevention and treatment of coronary artery disease (CAD). We hypothesized that individually tailored home-based exercise prescriptions will increase long-term PA and maximal exercise capacity among CAD patients without and with type 2 diabetes (CAD+T2D).

Methods: Physical activity of patients with CAD (n = 44) and CAD+T2D (n = 39), matched by age, sex and ejection fraction, was measured over 5 days with an accelerometer pre- and postexercise prescription. PA was assessed as the average time per day of moderate (METs = 2–5) and high (METs > 5) intensities. Six-month exercise prescriptions were introduced based on individual maximal heart rate reserve.

Results: At the baseline, patients with CAD+T2D engaged in less moderate-intensity PA (2:40 ± 1:23 versus 3:24 ± 1:17 h, P = 0·014) and exhibited a non-significant trend to reduced high-intensity PA (2:08 ± 2:57 versus 5:02 ± 9:19 min, P = 0·091) compared with patients with CAD. High-intensity PA increased markedly in CAD (5:02 ± 9:19 versus 9:59 ± 15:03 min) and patients with CAD+T2D (2:08 ± 2:57 versus 6:14 ± 10:18 min) after exercise prescription (main effect for time P = 0·001). Also maximal exercise capacity increased in both groups (main effect for time P<0·001).

Conclusion: Patients with CAD with T2D are physically less active than CAD patients without diabetes in their daily life. Individually tailored home-based exercise prescriptions are an effective way to promote more active lifestyles and improve fitness in both patient groups.

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Accepted for publication

Received 06 September 2011; accepted 31 May 2012

Key words

accelerometer; cardiac patients; exercise intensity; fitness; physical training

Introduction

Type 2 diabetes (T2D) is a common worldwide disease and a marked independent risk factor for coronary artery disease (CAD) and cardiovascular mortality (Haffner *et al.*, 1998; Decode Study Group, 2001; Vaccaro *et al.*, 2004; Junttila *et al.*, 2010). Diabetic patients with a previous myocardial infarction have a higher risk of premature mortality (Haffner *et al.*, 1998; Decode Study Group, 2001) and sudden cardiac death (Decode Study Group, 2001; Junttila *et al.*, 2010) compared with non-diabetic patients with a myocardial infarction.

Regular physical activity (PA) is highly recommended for both CAD (Miller *et al.*, 1997; Jolliffe *et al.*, 2001; Taylor *et al.*, 2004) and CAD+T2D patients (Thomas *et al.*, 2006; Colberg *et al.*, 2010). It is well established that long-term PA and exercise improve various health indices, such as cholesterol levels, blood pressure and cardiorespiratory fitness, in both patient groups (Hambrecht *et al.*, 1993; Miller *et al.*, 1997; Taylor *et al.*, 2004) and reduce the risk of cardiovascular and all-cause mortality (Jolliffe *et al.*, 2001; Taylor *et al.*, 2004; Moholdt *et al.*, 2008). Regular PA also has a positive influence on blood glucose control and insulin sensitivity in patients with diabetes (Boule *et al.*, 2001; Snowling & Hopkins, 2006; Thomas *et al.*, 2006; Colberg *et al.*, 2010).

Despite the well-known health benefits of regular PA and exercise, the majority of patients with CAD or T2D does not regularly engage in PA and do not meet the PA guidelines (Hays & Clark, 1999; Nelson *et al.*, 2002; Thomas *et al.*, 2004;

Plotnikoff *et al.*, 2006; Morrato *et al.*, 2007; Wofford *et al.*, 2007; Zhao *et al.*, 2008). Moreover, CAD patients with T2D are less likely to comply with PA recommendations than their counterparts without T2D (Zhao *et al.*, 2008) partly because of diabetes-related comorbidity, for example, obesity and physical disabilities (Gregg *et al.*, 2000; Plotnikoff *et al.*, 2006; Zhao *et al.*, 2011). Rehabilitation programmes and lifestyle interventions including PA counselling have been shown to be an effective way of promoting PA among patients with CAD or T2D (Di Loreto *et al.*, 2003; The Vesthold Heartcare Study Group, 2003; Kirk *et al.*, 2004; Oliveira *et al.*, 2008; Balducci *et al.*, 2010; Yohannes *et al.*, 2010). However, many cardiac patients do not attend recommended rehabilitation programmes (Farley *et al.*, 2003; Worcester *et al.*, 2004; Higgins *et al.*, 2008) and among patients attending programme the drop-out rate has shown to be 20–40% (Sanderson *et al.*, 2003; Worcester *et al.*, 2004; Yohannes *et al.*, 2007).

Long-term PA is difficult to measure precisely, and many prior studies contain weaknesses in reliable assessment of daily PA. Several studies have found an association between tested PA questionnaires and health variables, but the reliability and validity of self-administered questionnaires is weak (Forsen *et al.*, 2010). Self-report questionnaires on PA suffer from reporting bias, tending to overestimate PA levels (Troiano *et al.*, 2008; Boon *et al.*, 2010). Therefore, this study was designed to investigate the amount of PA among patients with CAD+T2D and age-matched CAD patients with a new accelerometer technique integrated into a wristwatch. We hypothesized that patients with CAD+T2D are less active than patients with CAD because of diabetes-related comorbidity. Secondly, we tested the hypothesis that individually tailored home-based exercise prescriptions will increase long-term PA and maximal exercise capacity among CAD patients with and without T2D.

Methods

Subjects and study protocol

This study is part of the ARTEMIS (Innovation to Reduce Cardiovascular Complications of Diabetes at the Intersection) study which has been registered at ClinicalTrials.gov, Record 1539/31/06. The patients in the ARTEMIS study have been recruited from a consecutive series of CAD patients with and without T2D (1:1 matched in terms of age, sex, prior myocardial infarction and revascularization procedure, Table 1) who underwent coronary angiography in the Division of Cardiology of the Oulu University Hospital. The ARTEMIS exercise prescription sub-study is a 2-year randomized and controlled exercise prescription trial for patients with CAD+T2D and CAD. In this study, we report PA data and the effects of exercise prescription during the first six months. CAD and its severity were assessed by measurement of the Syntax score from the coronary angiography (Sianos *et al.*, 2005). T2D was defined according to the WHO, 1999 (WHO, 1999) criteria. Patients who had a fasting plasma glucose level $\geq$ 7·0 mmol l^{-1} or were on hypoglycaemic medication based on prior diagnosis of diabetes were classified as having T2D. Patients without T2D were normoglycemic, defined as a plasma glucose level < 6·1 mmol l^{-1} in the fasting state and a plasma glucose level < 8·8 mmol l^{-1} during a two-hour glucose tolerance test.

Patient selection for this study is presented in Fig. 1. There were 346 patients with CAD and 461 patients with CAD+T2D in the ARTEMIS database. Of those patients, 497 (198 patients with CAD and 299 patients with CAD+T2D) were excluded from the exercise prescription study owing to the following criteria: advanced age (>75 years), body mass index (BMI) >40 kg m^{-2}, NYHA class III or IV, left ventricular ejection fraction (LVEF) <40%, scheduled cardiac revascularization therapy, heart failure, unstable angina pectoris, severe peripheral atherosclerosis, diabetic retinopathy or neuropathy or other inability to perform regular home-based exercise, for example, because of musculoskeletal problems. Altogether 224 out of 310 suitable patients (72%) were willing to participate and 113 of those patients (51 patients with CAD and 62 patients with CAD+T2D) were randomly selected into the exercise prescription group and 111 into a control group. Patients who did not want to (n = 16) or did not properly carry out the PA measurement (n = 7) and patients who did not participate in the 6-month follow-up measurements (n = 7) were excluded. In total, 44 patients with CAD, and 39 patients with CAD+T2D were included in the analyses of this study.

The following laboratory measurements were performed in the Department of Exercise and Medical Physiology at Verve (Oulu, Finland): body composition, glycated haemoglobin (HbA1c) level (Afinion^{TM} AS100, Axis-Shield PoC AS, Oslo, Norway) and blood pressure (average of two measures) in a supine position after a 10-min resting period (Tango, SunTech, Raleigh, NC, USA). The subjects performed a maximal exercise test on a bicycle for assessment of peak oxygen uptake (VO_{2peak}). The subjects were not allowed to eat or drink coffee for 3 h before the tests. Strenuous PA and use of alcohol were prohibited during the test day and on the preceding day. All the measurements were repeated after the 6-month exercise prescription. The study was performed according to the Declaration of Helsinki, and the local committee of research ethics of the Northern Ostrobothnia Hospital District approved the protocol, and all the subjects gave written informed consent.

Assessment of peak oxygen uptake

The patients performed an incremental symptom-limited maximal exercise test on a bicycle ergometer (Monark Ergomedic 839 E, Monark Exercise AB, Vansbro, Sweden) with 15-lead ECG recordings (GE Healthcare, CAM-14, Freiburg, Germany). The test was started at 30 W, and the work rate was increased by 15 W in men and 10 W in women every minute until voluntary exhaustion or ST depression > 0·2 mV in ECG.

Table 1 Characteristics of the study groups.

		CAD (n = 44)	CAD+T2D (n = 39)	P value between groups
Men/women		32/12	32/7	0·313
Age, year		62 ± 5	62 ± 5	0·692
Height, m		1·70 ± 0·08	1·72 ± 0·07	0·200
Weight, kg	Pre	78 ± 12	90 ± 13	<0·001
	Post	77 ± 11	90 ± 13	
BMI, kg/m^2	Pre	26·7 ± 3·1	30·4 ± 3·9	<0·001
	Post	26·4 ± 2·9	30·2 ± 3·9	
Waist-hip ratio	Pre	0·94 ± 0·08	1·00 ± 0·06	<0·001
	Post	0·94 ± 0·07	0·99 ± 0·06	
Systolic BP, mmHg	Pre	137 ± 17	135 ± 13	0·615
	Post	131 ± 14	135 ± 13	
Diastolic BP, mmHg	Pre	82 ± 8	81 ± 10	0·860
	Post	80 ± 7	79 ± 8	
HbA1c,%	Pre	5·5 ± 0·2	5·8 ± 0·5	<0·001
	Post	5·5 ± 0·2	5·9 ± 0·5	
History of AMI				
NSTEMI		16 (36%)	11 (28%)	0·428
STEMI		6 (14%)	9 (23%)	0·265
Revascularization				
PCI		24 (55%)	26 (67%)	0·260
CABG		11 (25%)	11 (28%)	0·741
SYNTAX score		3·2 ± 4·0	5·8 ± 7·0	0·115
EF,%		66 ± 7	67 ± 8	0·765
CCS class		1·1 ± 0·3	1·3 ± 0·6	0·078
Current smokers		4 (9%)	2 (5%)	0·487
Medication				
Oral antidiabetics		0 (0%)	30 (77%)	<0·001
Insulin		0 (0%)	5 (13%)	0·013
Beta blockers		34 (77%)	37 (95%)	0·023
ACEI/ARB		21 (48%)	25 (64%)	0·134
Statin		39 (89%)	37 (95%)	0·308
Anticoagulants		42 (95%)	38 (97%)	0·629
Calcium antagonist		4 (9%)	13 (33%)	0·006
Nitrates		4 (9%)	15 (38%)	0·001
Diuretics		8 (18%)	17 (44%)	0·012

Values are means ± SD; n, number of subjects; CAD, coronary artery disease; T2D, type 2 diabetes; BMI, body mass index; BP, blood pressure; HbA1c, glycated haemoglobin; AMI, acute myocardial infarction; NSTEMI, no-ST segment elevation myocardial infarction; STEMI, ST segment elevation myocardial infarction; PCI, percutaneus coronary intervention; CABG, coronary artery by-pass grafting; SYNTAX score, a lesion-based angiographic score after revascularization; EF, ejection fraction; CCS, Canadian Cardiovascular Society angina classification; ACEI, angiotensin conversion enzymes inhibitor; ARB, angiotensin receptor blocker; ACEI/ARB, patients using at least one of them.

Ventilation and gas exchange (M909 Ergospirometer, Medikro, Kuopio, Finland) were monitored continuously during the test. The highest 1-min mean value of oxygen consumption was expressed as VO_{2peak}. Maximal workload (W) and maximal metabolic equivalents (METs) were calculated as the average workload and METs during the last minute of the test.

Assessment of physical activity

PA was measured over five consecutive days during waking hours with a wristwatch equipped with a one-dimensional accelerometer (Polar AW200 Activity Watch; Polar Electro Oy, Kempele, Finland). Accelerometer technology has been recently validated and compared with energy expenditure measured by indirect calorimetry (Brugniaux *et al.*, 2010). According to previous studies (Gretebeck & Montoye, 1992; Trost *et al.*, 2005), 5 days of PA monitoring including weekend days is enough to make possible the reliable estimation of daily PA among adults. In present study PA measurement was started within 2 days after the laboratory measurements so that weekend days were included in the measurement days. Patients were advised to wear the accelerometer during all waking hours and carry on their normal daily routine.

Physical activity time (METs $\geq$ 2) per day was calculated at five different intensity levels and analysed separately for moderate (METs = 2–5, 'slow walking or walking') and high (METs > 5 'brisk walking or higher') intensity. Daily PA during waking hours was also expressed in average METs. Average METs were calculated as the patients mean daily energy expenditure (kcal) divided by his or her body weight divided by mean waking hours per day. One MET corresponds to an energy expenditure of approximately 1 kcal per kilogram

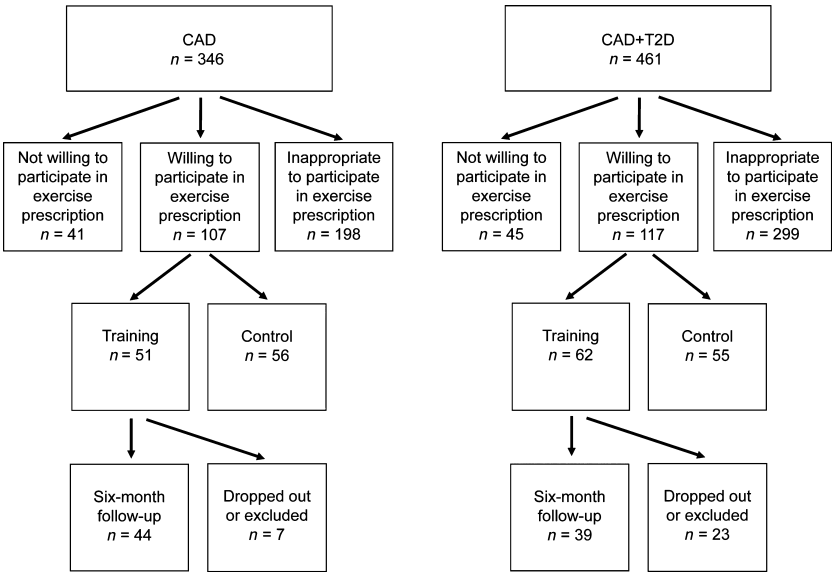

Figure 1 Patient's selection protocol from the ARTEMIS database.

of body weight per hour, or an oxygen uptake of 3·5 $ml \cdot kg^{-1} \cdot min^{-1}$. Reassessment of PA was made during 5 consecutive days including weekend days after the completion of the 6-month exercise period.

Exercise prescription

The controlled 6-month exercise prescription was based on current guidelines (Piepoli *et al.*, 2010) and consisted of home-based endurance training (30 min) and strength training (30 min). During the first 3 months the exercise prescription was four heart-rate-controlled exercise sessions per week; three endurance training and one strength training session. The intensity of the endurance training was stated as between 50% and 60% of the heart rate reserve, using a heart rate recorder (Polar F1, Polar Electro Oy, Kempele, Finland). After 3 months, the exercise prescription was five exercise sessions per week, two endurance training sessions at 50–60% of the heart rate reserve, two endurance training sessions at 60–70% of the heart rate reserve and one home-based strength training session.

Exercise prescription was introduced after baseline laboratory and PA measurements by specialist of sports medicine or physiotherapist specialized in cardiac rehabilitation in the Department of Exercise and Medical Physiology at Verve (Oulu, Finland). The patients got a daily diary which was marked training days and resting days. The target duration of exercise sessions and the actual training heart rate zones were included in the diary. The patients also got oral and written instructions how to use the HR recorder and how to write down the duration and the average heart rate of every training session in the diary. During 6-month exercise period the patients were contacted by specialist of sports medicine or physiotherapist in time point 1 and 3 months to check if there is problem with the adherence of exercise prescription or the use of HR recorder.

Weekly training load was calculated as the mean training impulse (TRIMP) using the following formula: $TRIMP = ABC$, in which A is exercise time (min), B is heart rate (proportionally to the heart rate reserve), and C is $e^{1 \cdot 92B}$ for men and $e^{1 \cdot 67B}$ for women (Morton *et al.*, 1990). Target TRIMP per week for endurance training and strength training was calculated using the same formula. Calculating target TRIMP for endurance training B was stated as an average of target heart rate (55% or 65% of the heart rate reserve) and in strength training B was defined as 90% of the target heart rate of light endurance training based on our previous experience (Hautala *et al.*, 2006). All the patients were included in the analysis regardless if their realized TRIMP were under or over the target TRIMP.

Statistical analyses

A Kolmogorov–Smirnov Z-test was used to examine the Gaussian distribution of the data. At the baseline, the groups were compared using a t-test for independent samples, a Mann-Whitney U–test, or a chi-square test, accordingly. Additionally, between-group comparisons in PA variables at preprescription conditions were adjusted for BMI and exercise capacity ($METs_{max}$), and exercise test variables were adjusted for BMI using ANCOVA. For variables having only baseline values and training realization (TRIMPs), a t-test for independent samples, a Mann–Whitney U–test, or a chi-square test was applied accordingly. The effects of the exercise prescription were analysed by two-factor ANOVA with time and interventions. When significant time × intervention interaction was observed, a *post hoc* analysis was performed using a paired t-test between pre- and postprescription values within each group and a t-test for independent samples for between-group comparisons at pre- and postprescription conditions. PA at high intensity was the only follow-up variable that had non-Gaussian distribution and was transformed into natural logarithm

before parametric statistical tests. Statistical analyses of the data were performed with SPSS software (SPSS 19.0, SPSS Inc., Chicago, IL, USA). Statistical significance was defined as a P-value <0·05 for all tests.

Results

Descriptive results

The characteristics of the study groups, including comparisons between groups, are presented in Table 1. The patients with CAD+T2D had a higher BMI than the patients with CAD ($P < 0·001$) and they had a higher HbA1c level ($P<0·001$ compared with the patients with CAD). Blood pressure, angiographic severity of CAD, ejection fraction or smoking habits did not differ between the groups (Table 1). The mean duration of diabetes was 72 ± 97 months. The history of acute myocardial infarction (AMI) did not differ between CAD+T2D and patients with CAD (Table 1). The mean duration between AMI and the begin of the study was 48 ± 57 months in CAD+T2D patients and 19 ± 21 months in patients with CAD ($P = 0·249$).

Beta blockers, calcium antagonists, nitrates and diuretics were more commonly used by the CAD+T2D than the patients with CAD (Table 1). During exercise prescription, 13 (30%) patients with CAD and 13 (33%) patients with CAD+T2D changed their medication ($P = 0·710$ between groups). Typically, the changes of medication concerned with the beta blocker (started 2 patients and reduced 8 patients), antiplatelet therapy (stopped in 6 patients) and angiotensin conversion enzymes inhibitor or angiotensin receptor blocker (increased 3 and reduced 3 patients).

Physical activity before exercise prescription

The mean waking time was 15:00 ± 1:20 h per day in patients with CAD+T2D and 15:15 ± 1:05 h per day in patients with CAD ($P = 0·338$). Before exercise prescription, total PA time per day was lower in the patients with CAD+T2D than in the patients with CAD (2:42 ± 1:23 versus 3:29 ± 1:18 h, $P = 0·010$) (Fig. 2a). Divided separately into moderate and high-intensity levels, the patients with CAD+T2D engaged in less moderate-intensity PA than the patients with CAD ($P = 0·014$) (Table 2) and they exhibited a non-significant trend to reduced high-intensity PA (2:08 ± 2:57 versus 5:02 ± 9:19 min, $P = 0·091$) (Fig. 2b). Average METs during waking hours were lower in the patients with CAD+T2D than in the patients with CAD ($P = 0·003$) (Table 2). However, differences in PA variables between groups did not remain statistically significant after adjustment for BMI and exercise capacity (Table 2, Fig. 2a,b).

Physical activity after exercise prescription

The effects of exercise prescription on PA are shown in Table 2 and Fig. 2a,b. There were no significant changes in total or moderate-intensity PA in either group (Table 2, Fig. 2a). However, high-intensity PA increased in the patients with CAD (from 5:02 ± 9:19 to 9:59 ± 15:03 min) and in the patients with CAD+T2D (from 2:08 ± 2:57 to 6:14 ± 10:18 min, main effect for time $P = 0·001$) (Fig. 2b). There was no main effect for time × group interaction in any PA variables in patients with CAD or CAD+T2D (Table 2, Fig. 2a,b).

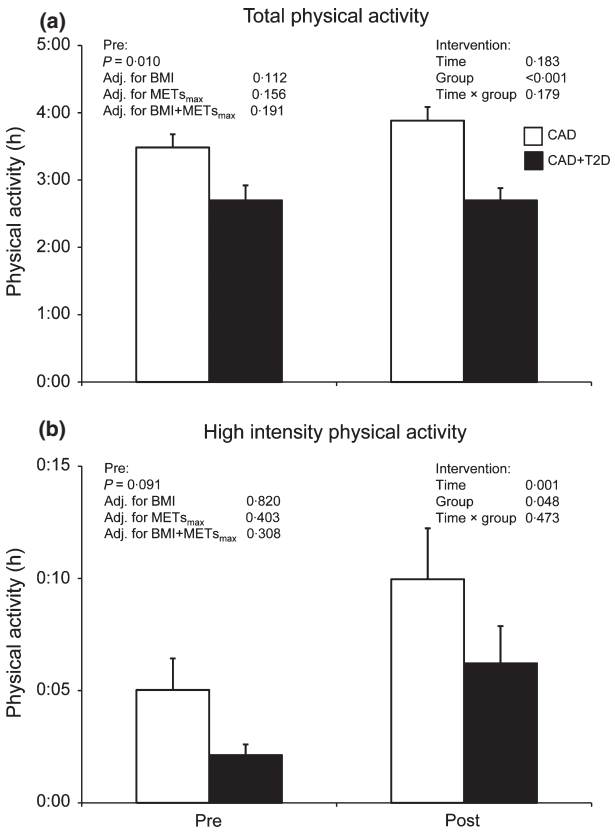

Figure 2 Changes in total (a) and high-intensity (b) physical activity between pre and postprescription measurements in coronary artery disease patients (CAD) and CAD patients with type 2 diabetes (CAD+T2D). Error bars indicate mean ± SE.

Adherence to exercise prescription

Adherence to the tailored exercise prescription, including comparisons between patient groups, is presented in Table 3. Targeted and realized TRIMPs did not differ between the patients with CAD and CAD+T2D at any condition. The weekly TRIMP of endurance training was significantly higher than the prescription during the first 3 months, but did not differ from the planned training TRIPMs during the last 3 months.

Maximal exercise test

The results of the maximal exercise test, including comparisons between groups, are given in Table 2. At the baseline the

Table 2 Physical activity and maximal exercise test of the study groups before and after exercise prescription.

Pre	CAD (n = 44)	CAD+ T2D (n = 39)	Adj. for BMI	Adj. for $METs_{max}$	Adj. for BMI+$METs_{max}$
Physical activity					
PA at moderate intensity, hour	3:24 ± 1:17	2:40 ± 1:23*	0·118	0·165	0·193
$METs_{av}$ per day	1·9 ± 0·4	1·7 ± 0·3**	0·132	0·159	0·249
Maximal exercise test					
max workload, W	159 ± 47	142 ± 36	0·348	–	–
HR_{max}, bpm	139 ± 19	128 ± 19*	0·125	–	–
$METs_{max}$	8·1 ± 2·0	6·5 ± 1·6**	0·198	–	–
$VO_{2peak,}$ $l \cdot min^{-1}$	2·11 ± 0·6	1·92 ± 0·5	0·181	–	–
$VO_{2peak,}$ $ml \cdot kg^{-1} \cdot min^{-1}$	27·2 ± 7·2	21·6 ± 5·7**	0·085	–	–

Post	CAD (n = 44)	CAD+ T2D (n = 39)	Time effect	Group effect	Interaction effect
Physical activity					
PA at moderate intensity, hour	3:43 ± 1:21	2:36 ± 1:06	0·418	<0·001	0·204
$METs_{av}$ per day	2·0 ± 0·5	1·7 ± 0·3	0·262	<0·001	0·577
Maximal exercise test					
max workload, W	162 ± 46†	151 ± 36†	<0·001	0·101	0·041
HR_{max}, bpm	139 ± 18	131 ± 19	0·217	0·015	0·189
$METs_{max}$	8·4 ± 1·9	6·9 ± 1·7	<0·001	<0·001	0·193
VO_{2peak}, $l \cdot min^{-1}$	2·16 ± 0·6	2·04 ± 0·5†	<0·001	0·190	0·039
VO_{2peak}, $ml \cdot kg^{-1} \cdot min^{-1}$	28·1 ± 6·8	23·2 ± 6·6	<0·001	<0·001	0·188

Values are means ± SD; n, number of subjects; CAD, coronary artery disease; T2D, type 2 diabetes; BMI, body mass index; PA, physical activity; $METs_{av}$, average value of metabolic equivalent measured during waking hours; HR, heart rate; VO_{2peak}, peak oxygen uptake; *P<0·05 and **P<0·01 between the groups without adjustments; †P<0·05 between pre and postmeasurements.

Table 3 Adherence to the exercise prescription in patients groups.

	CAD (n = 44)	CAD+T2D (n = 39)	P value between groups
Training 1–3 months			
Endurance training			
Target TRIMP per week	141 ± 38	146 ± 35	0·286
Realized TRIMP per week	212 ± 112	232 ± 131	0·465
P-level target versus realized	P<0·001	P<0·001	
Strength training			
Target TRIMP per week	22 ± 10	20 ± 10	0·082
Realized TRIMP per week	21 ± 31	24 ± 46	0·902
P-level target versus realized	P = 0·026	P = 0·011	
Training 4–6 months			
Endurance training			
Target TRIMP per week	225 ± 50	225 ± 54	0·956
Realized TRIMP per week	268 ± 160	278 ± 157	0·989
P-level target versus realized	P = 0·093	P = 0·204	
Strength training			
Target TRIMP per week	22 ± 10	20 ± 10	0·082
Realized TRIMP per week	17 ± 19	25 ± 55	0·240
P-level target versus realized	P = 0·002	P = 0·001	

Values are means ± SD; n, number of subjects; CAD, coronary artery disease; T2D, type 2 diabetes; TRIMP, training impulse.

patients with CAD+T2D had lower exercise capacity and lower maximal heart rate than the patients with CAD (Table 2), for example, the maximal heart rate was 128 ± 19 versus 139 ± 19 bpm for the CAD+T2D versus patients with CAD, respectively (P = 0·011). Differences in exercise capacity and maximal heart rate between groups did not remain statistically significant after adjustment for BMI. Maximal exercise capacity increased in both patients groups from 8·1 ± 2·0 to 8·4 ± 1·9 METs and from 6·5 ± 1·6 to 6·9 ± 1·7 METs for the patients with CAD and CAD+T2D, respectively (main effect for time P<0·001), but there was no main effect for time × group interaction in patients with CAD or CAD+T2D. Moreover, maximal workload and VO_{2peak} increased specially in patients with CAD+T2D, for example, VO_{2peak} from 1·92 ± 0·5

$l \cdot min^{-1}$ to 2·04 ± 0·5 $l \cdot min^{-1}$ (main effect for time $P<0·001$, main effect for time × group interaction $P = 0·039$) (Table 2).

Clinical variables

In clinical variables, main effect for time was observed in weight, BMI, systolic and diastolic blood pressure and HbA1c ($P<0·05$), but there was no main effect for time × group interaction in any clinical variables in patients with CAD or CAD+T2D (Table 1).

Discussion

The main finding of this study is that patients with CAD+T2D are physically less active than CAD patients without T2D, documented by objective measurement of daily PA. This difference is largely a result of obesity, i.e. higher BMI of patients with diabetes compared to their non-diabetic counterparts. Moreover, patients with CAD+T2D had lower cardiorespiratory fitness and maximal exercise capacity than age-matched patients with CAD. However, carefully tailored exercise prescriptions based on maximal exercise tests and individual heart rate zones resulted in increased high-intensity PA and exercise capacity in both patient groups.

Physical activity before exercise prescription

In the present study PA was investigated objectively with an accelerometer in CAD patients with and without T2D carefully matched by age, sex and ejection fraction. We found that patients with CAD+T2D are more passive than CAD patients without diabetes. Secondly, at the intensity of brisk walking or higher, the average time of PA was very low among both study groups. The recommendations for brisk walking or higher intensity is $\geq$ 30 min day^{-1} on $\geq$ 5 days $week^{-1}$ (Piepoli *et al.*, 2010), whereas we measured an average PA time/day of approximately 5 and 2 min at the intensity of brisk walking or higher for patients with CAD and CAD+T2D, respectively. The measured PA values are far from the recommendations for both groups.

In agreement with the present observations, previous studies based on questionnaires have shown that a majority of patients with CAD do not engage in recommended levels of PA (Nelson *et al.*, 2002; Lin *et al.*, 2004; Resnick *et al.*, 2006; Wofford *et al.*, 2007; Zhao *et al.*, 2008, 2011) and are physically more passive than the healthy population (Morrato *et al.*, 2007; Zhao *et al.*, 2008, 2011). Also, the prevalence of achieving the recommended PA level is significantly lower among CAD+T2D patients compared with their counterparts without T2D (Zhao *et al.*, 2008). In the present study, the average total PA time per day was almost 50 min less in CAD +T2D patients than in CAD patients without T2D. Taken together, our results suggest that it is necessary to develop more intensive PA counselling for patients with CAD populations with or without diabetes.

Physical activity after exercise prescription

Our data showed that controlled 6-month exercise prescriptions increased particularly high-intensity PA among CAD patients with and without T2D. Similarly, increased levels of high-intensity PA, measured by a questionnaire, have been observed during a 3-month home-based cardiac rehabilitation programme (Blanchard *et al.*, 2010). Previous studies have shown that high-intensity exercise is more effective in increasing cardiorespiratory fitness (Oberman *et al.*, 1995; O'Donovan *et al.*, 2005), ventilatory threshold (Jensen *et al.*, 1996), and left ventricular ejection fraction (Oberman *et al.*, 1995) than low-intensity exercise in men with CAD. Improvements in maximal oxygen uptake are higher in high-intensity exercise than in low-intensity exercise, regardless of equal energy cost (O'Donovan *et al.*, 2005). Therefore, our findings that patients with CAD increased their high-intensity PA by 50% during exercise prescription can be considered clinically relevant.

In patients with diabetes, high-intensity PA seems to be associated with a lower incidence of acute coronary events, whereas low-intensity PA has no significant association with development of acute coronary events (Makrilakis *et al.*, 2004). It has been shown that higher-intensity exercise training also produces greater improvement in maximal oxygen uptake and HbA1c in patients with diabetes (Boule *et al.*, 2003). In addition, the duration of high-intensity activities is an important component in current PA recommendations for CAD patients with T2D (Piepoli *et al.*, 2010).

Clinical variables after exercise prescription

In patients with T2D, exercise training improves cardiorespiratory fitness (Boule *et al.*, 2003) and has a positive influence on blood glucose control (Boule *et al.*, 2001; Snowling & Hopkins, 2006; Thomas *et al.*, 2006; Colberg *et al.*, 2010). We found that a controlled 6-month exercise prescription is an effective way to increase cardiorespiratory fitness, defined as VO_{2peak}, among patients with CAD+T2D. Interestingly, we did not find a statistically significant decrease in HbA1c in patients with diabetes during the exercise prescription. This finding may be partly related to the fact that the patients in the present study have good control of their blood glucose level and their HbA1c levels at the baseline were lower on average compared with patients with diabetes in previous studies (6·0 ± 0·7 versus 8·9 ± 1·8%, respectively) (Boule *et al.*, 2001; Snowling & Hopkins, 2006).

Some previous studies have shown that exercise is beneficial for weight reduction in patients with T2D (Agurs-Collins *et al.*, 1997; Balducci *et al.*, 2010). However, no differences in body weight changes were observed between the exercise and control group in a meta-analysis (Boule *et al.*, 2001). In the present study, we did not find significant reduction in BMI in patients with CAD+T2D suggesting that exercise alone without

dietary counselling may not be enough for weight reduction of obese T2D patients with CAD. In line with this observation, the baseline PA differences between patients with CAD and CAD+T2D did not remain significant after adjustment for BMI. This may indicate that differences in PA are more related to overweight than T2D.

Methodological considerations

Self-report questionnaires on PA are an easy and inexpensive way to collect information on PA among a large study population. However, it is well known that the reliability and validity of self-administered questionnaires is weak, particularly for the elderly (Forsen *et al.*, 2010), and questionnaires commonly tend to overestimate PA levels (Troiano *et al.*, 2008; Boon *et al.*, 2010). Accelerometers are more reliable tools than questionnaires for measuring PA levels objectively (Troiano, 2005). The most commonly used accelerometers are carried beside the hip or waist during the measurements (Ward *et al.*, 2005; Garatachea *et al.*, 2010), and therefore the main limitation of these accelerometers is the impossibility to detect upper body movements, which are common in the elderly during everyday activities (Garatachea *et al.*, 2010). In the present study, we used new technology where an accelerometer is integrated into a wristwatch, making it very easy to use. Secondly, the device is able to measure separate PA times, even at five different exercise intensities, which gives new perspectives in studying daily PA times among various populations. The device used in the present study was also recently validated against indirect calorimetry (Brugniaux *et al.*, 2010) and showed very high accuracy in detecting PA times at different intensities. Maximal exercise capacity is rather low for cardiac patients, and therefore it was more practical to analyse PA at only two different intensities, expressed as moderate (2–5 METs) and high intensity (>5 METs).

Limitations

In the present study PA was measured as time spent at different absolute intensity levels, expressed as moderate (2–5 METs) and high intensity (>5METs). Our PA measurements did not take into account the variations on subjects' individual fitness levels. An activity requiring a high-intensity PA level (METs >5) may command almost maximal effort among patients with a lower fitness level.

A high number of patients were excluded from the exercise prescription programme in the present study (57% of patients with CAD and 65% of patients with CAD+T2D). All these patients were excluded owing to advanced age or serious co-morbidities. Our exercise prescription was home-based and rather intensive, including almost daily exercise training sessions, and it excluded patients who may not be able to perform the prescription because of contraindication for exercise, for example, severe chest pain or arrhythmias during or postexercise (Frolkis *et al.*, 2003; Dewey *et al.*, 2008).

Moreover, 26% of the patients with CAD and 29% of the patients with CAD+T2D were not willing to participate in the exercise training prescription even though they met the inclusion criteria. There may be various obstacles to participating in the exercise prescription like lack of motivation, depression, or fear of exercise after a cardiac event. The health care system should be able to tackle these obstacles better in future studies, and most importantly, in daily practice.

Finally, 37% of patients with CAD+T2D and 14% of patients with CAD were excluded from the analyses because of incomplete PA measurement at the baseline or interruption of exercise intervention before postprescription measurements. It is necessary take into account that most of the excluded patients (77%), especially among patients with CAD+T2D, had problems with the PA measurement. Even though our accelerometer was integrated into a wristwatch, making it very easy to use, many elderly patients were still unwilling or uncertain how to use this technical device. However, only 8% of patients with CAD+T2D and 4% of patients with CAD interrupted exercise training before postprescription measurements mainly because of musculoskeletal problems or lack of motivation. These drop-out rates are remarkably less than those that have been reported in previous studies (Worcester *et al.*, 2004; Yohannes *et al.*, 2007).

Conclusions

Our results showed that a controlled 6-month exercise prescription is an effective way to increase objectively measured high-intensity PA among CAD patients with and without T2D. We also found that PA at the intensity of 'brisk walking or higher' is very low among all CAD patients with and without diabetes. This indicates that there is a need to develop a more intensive PA counselling strategy for cardiac and diabetic patients.

Acknowledgments

The authors would like to thank RN Pirkko Huikuri, RN Päivi Koski, RN Päivi Kastell, and RN Sari Kaarlenkaski for their excellent assistance in this study. This study is partly funded by Finnish Technology Development Centre (TEKES, Helsinki, Finland), Polar Electro Oy (Kempele, Finland) and Hur Oy (Kokkola, Finland).

Conflict of interest

The authors declare that they have no conflict of interest.

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